extension of time fees or other relief as may be required, or credit any overpayment to Deposit Account No. 06-1300 (Our File A-68087-1/RMS/DCF/AMS).

IN THE CLAIMS

Please cancel Claims 1-16, without prejudice or disclaimer.

Please add the following new claims:

--17. A method comprising:

a) providing a hybridization complex comprising

i) a first target sequence comprising

1) a first nucleotide at a detection position; and

2) a first label specific to said first nucleotide at said detection position;

ii) a capture probe attached to a microsphere on a surface of a substrate; and

b) detecting said label to identify said first nucleotide at said detection position.

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18. The method according to claim 17 wherein said first target sequence comprises an adapter sequence and said adapter sequence is hybridized to said capture probe.

19. The method according to claim 17 further comprising:

a) providing a second target sequence comprising a first domain and a second domain comprising said detection position;

b) hybridizing a first ligation probe to said first domain and a second ligation probe to said second domain of said second target sequence wherein if said second ligation probe comprises a nucleotide that is

perfectly complementary to said detection position a ligation structure is formed;

c) ligating said ligation structure to form said first target sequence.

20. The method according to claim 19, wherein said first ligation probe comprises an adapter sequence and said second ligation probe comprises said first label.

21. The method according to claim 17 further comprising:

a) providing a second target sequence comprising said detection position;

b) hybridizing an extension primer adjacent to said detection position;

c) adding a polymerase enzyme and at least a first dNTP comprising a covalently attached detectable label under conditions whereby if said first dNTP basepairs with the nucleotide at said detection position, said extension primer is extended by said enzyme to incorporate said label into said extension primer to form said first target sequence.

22. The method according to claim 21, further comprising adding a second dNTP, wherein said first and second dNTPs comprise first and second labels, respectively.

23. The method according to claim 22, wherein at least said first label comprises a fluorophore.

24. The method according to claim 22, wherein at least said first label comprises biotin.

25. The method according to claim 24, wherein at least said first label comprises imine-biotin.

26. The method according to claim 22, wherein said at least said first dNTP comprises

a functional group for addition of a fluorophore.

27. The method according to claim 17 further comprising:

a) providing a second target sequence comprising 5' to 3':

i) a first target domain comprising an overlap domain comprising at least a nucleotide in the detection position; and

ii) a second target domain contiguous with said detection position;

b) hybridizing:

i) a first probe to said first target domain; and

ii) a second probe to said second target domain, wherein said second probe comprises:

1) a detection sequence that does not hybridize with said target sequence; and

2) a detectable label;

wherein if said second probe comprises a nucleotide that is perfectly complementary to said detection position a cleavage structure is formed; and

c) contacting said cleavage structure with a cleavage enzyme to cleave said detection sequence to form said first target sequence.

28. The method according to claim 19, 21 or 27, wherein said first target sequence comprises an adapter sequence and said adapter sequence is hybridized to said capture probe.

29. The method according to claim 17, 19, 21 or 27, wherein said substrate is a fiber optic bundle.

30. The method according to claim 17, 19, 21 or 27 wherein said substrate is selected

from the group consisting of glass and plastic.

31. The method according to claim 17, 18, 19, 21 or 27, wherein said first label is a fluorophore.

32. A method of determining the identification of a nucleotide at a detection position in a target sequence comprising:

a) providing a hybridization complex comprising a target sequence and at least a first probe;

b) adding a composition comprising a nucleotide that hybridizes with the nucleotide at said detection position and an enzyme that alters said probe when said nucleotide hybridizes with said nucleotide at said detection position to form an altered probe, wherein said altered probe comprises a label specific to said nucleotide;

c) forming an assay complex with said altered probe and a capture probe covalently attached to a microsphere on a surface of a substrate; and

d) determining the nucleotide at said detection position by detecting said label.

33. A method of determining the identification of a nucleotide at a detection position in a target sequence comprising:

a) providing a hybridization complex comprising a target sequence, at least a first probe and a capture probe covalently attached to a microsphere on a surface of a substrate;

b) adding a composition comprising a nucleotide that hybridizes with said detection position and an enzyme that alters said first probe when said nucleotide hybridizes with said detection position to form an altered probe, wherein said altered probe comprises a label specific to said nucleotide;

and

d) determining the nucleotide at said detection position by detecting said label.

34. A method of determining the identification of a nucleotide at a detection position in a target sequence comprising:

a) providing a hybridization complex comprising a target sequence and a capture probe covalently attached to a microsphere on a surface of a substrate;

b) adding a composition comprising a nucleotide that hybridizes with said detection position and an enzyme that alters said capture probe when said nucleotide hybridizes with said detection position to form an altered capture probe, wherein said altered capture probe comprises a label; and

d) determining the nucleotide at said detection position by detecting said label.

35. The method according to claim 32, 33 or 34, wherein said label is a fluorophore.

36. The method according to claim 32, 33 or 34, wherein said nucleotide is a first dNTP comprising a first label and said enzyme is a polymerase, whereby when said first dNTP basepairs with the nucleotide at said detection position, said first probe is extended by said enzyme to incorporate said first label into said first probe.

37. The method according to claim 32, 33 or 34, wherein said composition comprises a second probe comprising said nucleotide wherein said second probe hybridizes with said target sequence, said nucleotide basepairs with said detection position and said enzyme is a ligase, whereby when said nucleotide basepairs with said nucleotide at said detection position, a ligation structure is formed and said ligase ligates said ligation

structure.

38. A method of determining the identification of a nucleotide at a detection position in a target sequence comprising:

a) providing a hybridization complex comprising said target sequence and a capture probe covalently attached to a microsphere on a surface of a substrate; and

b) contacting said microsphere with a plurality of detection probes each comprising:

i) a unique nucleotide at the readout position; and

ii) a unique detectable label; and

c) detecting a signal from at least one of said detectable labels to identify the nucleotide at the detection position.

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39. A method of determining the identification of a nucleotide at a detection position in a target sequence comprising:

a) providing a hybridization complex comprising said target sequence, wherein said target sequence comprises a first target domain directly 5' adjacent to said detection position, a capture probe covalently attached to a microsphere on a surface of a substrate, and an extension primer hybridized to said first target domain of said target sequence;

b) contacting said microsphere with:

i) a polymerase enzyme;

ii) a plurality of dNTPs each comprising a covalently attached detectable label;

under conditions whereby if one of said dNTPs basepairs with the nucleotide at said detection position, said extension primer is extended by said enzyme to incorporate said label; and

c) identifying the nucleotide at said detection position.

40. A method of determining the identification of a nucleotide at a detection position in a target sequence comprising a first target domain comprising said detection position and a second target domain adjacent to said detection position, said method comprising:

a) hybridizing a first ligation probe to said first target domain;

b) hybridizing a second ligation probe to said second target domain, wherein if said second ligation probe comprises a nucleotide that is perfectly complementary to said detection position a ligation structure is formed;

c) ligating said first and said second ligation probes to form a ligated probe;

d) forming an assay complex with said ligated probe, a capture probe covalently attached to a microsphere on a surface of a substrate, and at least one label;

e) detecting the presence or absence of said label as an indication of the formation of said ligation structure; and

f) identifying the nucleotide at said detection position.

41. A method of determining the identification of a nucleotide at a detection position in a target sequence wherein said target sequence comprises 5' to 3':

a) a first target domain comprising an overlap domain comprising at least a nucleotide in the detection position; and

b) a second target domain contiguous with said detection position;

said method comprising:

i) providing a hybridization complex, wherein said hybridization complex comprises:

1) a first probe hybridized to said first target domain; and

2) a second probe hybridized to said second target domain, wherein said second probe comprises:

i) a detection sequence that does not hybridize with said target sequence; and

ii) a detectable label;

wherein if said second probe comprises a nucleotide that is perfectly complementary to said detection position a cleavage structure is formed;

ii) contacting said hybridization complex with a cleavage enzyme that will cleave said detection sequence;

iii) forming an assay complex with said detection sequence, a capture probe covalently attached to a microsphere on a surface of a substrate, and at least one label; and

iv) detecting the presence or absence of said label as an indication of the formation of said cleavage structure, whereby the nucleotide at said detection is identified.--

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REMARKS

Claims 17-41 are pending. Support for new claims is found throughout the specification and in the claims is filed. Support for claim 17 is found at p. 10, lines 23-29 and in claim 1 as filed. Support for new claims 18 and 28 is found at p. 42, lines 10-19. Support for new claims 19, 32, 33, 34, 37 and 40 is found at p. 29, lines 30-37 and claim 15 as filed. In addition, claims 32, 33 and 34 find support at p. 18, lines 2-8. Support for claim 20 is found at p. 42, lines 10-19 and p. 29, lines 11-12. Support for claims 21, 22, 32, 33, 34, 36 and 39 is found at p. 12, lines 30-31, p. 18, lines 10-17 and claim 6 as filed. Support for claim 23 is found in claim 7 as filed. Support for claim